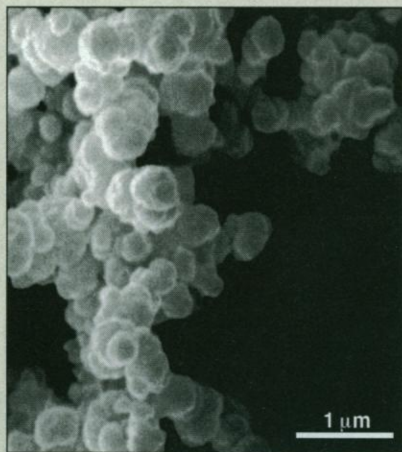
Finding Life's Limits

WASHINGTON, D.C.—Everything in life is getting smaller, it seems—computers, telephones, camcorders. Even cells seem to be shrinking, with reports of tiny, ancient microbes on Mars (see main text) and claims of so-called "nannobacteria" on Earth—putative cells occupying only 0.01% of the volume of a typical *Escherichia coli* bacterium. But unlike computer chips that shrink as they are reinvented with new materials, all life on Earth seems to use the same standard parts. Those components—DNA, RNA, and the ribosomes that help translate the genetic code into proteins—have a fixed size.

That puts a limit on how small a self-replicating cell can be, according to a group of experts from physics, biochemistry, ecology, and microbiology who gathered at the National Academy of Sciences last month* to discuss the limits of life at the tiniest level. Assuming that a cell needs DNA and ribosomes to make its proteins, a spherical cell much smaller than about 200 nanometers (nm) in diameter—about one-tenth the diameter of an *E. coli*—"is not compatible with life as we know it," says cell biologist Christian de Duve of the Christian de Duve Institute of Cellular Pathology in Brussels and The Rockefeller University in New York City. Only radical new biology could relax these size limits, he and his colleagues concluded.



Beyond the limit? Kajander sees bacteria as small as 50 nm in images like this one.

One of the claims prompting this exploration of the limits of small came from geologist Robert Folk of the University of Texas, Austin. He reported finding tiny bacteria-like objects as small as 30 nm across—which he calls "nannobacteria"—in everything from tapwater to tooth enamel (*Science*, 20 June 1997, p. 1777). Then there were the putative martian microbes, as small as 20 nm by 100 nm, and a Finnish report of bacteria smaller than 100 nm—their term is "nanobacteria"—cultured from human and cattle blood.

Such dimensions do not leave enough room for the basic set of genes needed for life, said workshop participants. By identifying the genes shared by the simplest organisms, researchers have recently concluded that at least 250 or so are required for survival as a self-replicating cell. That's about half the number present in the smallest known bacterial genome. (Viruses, which can't replicate on their own, can be smaller.) The DNA needed for 250 genes would just about fill a sphere 100 nm in diameter; add enough room for ribosomes (each of which is 20 nm in diameter), for the DNA to unwind for replication, and for chemical reactions of the cell, and 200 nm is needed. At 50 nm in diameter, biochemist Michael Adams of the University of Georgia, Athens, calculated, a spherical cell would have room for two ribosomes, 260 proteins, and only eight genes' worth of DNA.

Even with 250 genes, cells would have to be parasites, relying on ready-made nutrients from their hosts. "By the time you get to an organism of this size," said biochemist Peter Moore of Yale University, "you are either an obligate parasite or you have a standing order at [the biological supply house] SIGMA." If the putative fossils from Mars were free-living, they "would have to reflect a biochemistry unlike any we know," he said.

But biochemist and physician Olavi Kajander of the University of Kuopio in Finland says he has organisms that prove the theoretical limits wrong. He says that although the nanobacteria he has cultured from blood and urine are mostly between 200 and 500 nm, he can get viable cultures after passing them through a 100-nm filter. He also claims to see spheres as small as 50 nm in diameter under the electron microscope.

Kajander argues that his smallest particles, if not viable alone, might join together to make a reproducing organism. He adds that perhaps they can get along with less, growing so slowly that they need few ribosomes, for example. As for Folk, he is still finding 40-nm, bean-shaped "cells" in electron micrographs that he believes are biological, although they may be "some sort of new life-form."

Other scientists at the meeting were doubtful. "It's really easy to get fooled," says microbiologist Don Button of the University of Alaska, Fairbanks. Cells larger than 100 nm might have squeezed through Kajander's filter, he says, and the preparation process for electron microscopy sometimes shrinks cells. Paleontologist Andrew Knoll of Harvard University agrees. "I think everyone pretty much agreed that ... nothing much smaller than 200 nm is likely to be viable."

Still, researchers admit that unknown kinds of life-forms might not face the same limits. Before DNA, ribosomes, and proteins, there must have been simpler life-forms. With a single molecule capable of both replicating itself and catalyzing reactions—such as RNA, for example—a cell would need far less space, several scientists told the meeting. A sphere 50 nm across could comfortably contain the 50 or so catalytic "genes" necessary for self-replication and basic metabolism, with plenty of room left over for chemical reactions, chemist Steve Benner of the University of Florida, Gainesville, said.

If such primitive life-forms once existed here, they were outcompeted by the more complex forms now populating Earth, but they might exist elsewhere. "We really have no assurance that our biology exhausts the possibilities for life in the universe," says Knoll. But until a persuasive sample of such life is discovered, earthly and extraterrestrial nanocandidates will face tough scientific scrutiny.

—**GRETCHEN VOGEL**

* Workshop on Size Limits of Very Small Microorganisms, 22–23 October.

CREDIT: O. KAJANDER/UNIVERSITY OF KUOPIO

bar). And at the Houston workshop, McKay went part of the way toward accepting that limit. Anything smaller in volume than a 100-nanometer sphere "we simply don't believe is indicative of bacteria," he said. That criterion eliminates the objects in the *Science* paper as well as "The Worm," which is 250 nanometers long but too slender to make the cut. McKay also ruled out the phalanxes of worms, agreeing that, as another group argued last year, they are merely the jutting edges of mineral crystals reshaped by a coating used to prepare the sample for the scanning electron microscope (*Science*, 5 December 1997, p. 1706).

But McKay wouldn't write off the bacteria-like forms completely, saying that they "may very well be parts of bacteria from Mars." And as for intact bacteria, "we think there are large objects that are still candidates," he said, although he declined to offer any examples. "Until we get our data straightened out, that's all I want to say."

Even if McKay's team does come up with larger examples, few researchers are likely to be persuaded by simple bacteria-like shapes. Inorganic deposition can take such lifelike forms that shape alone proves little, say paleontologists and mineralogists. "Unfortunately, nature has a perverse sense of humor," ex-